AD-A132 618 HEAT EXCHANGE FOLLOWING ATROPINE INJECTION BEFORE AND AFTER HEAT ACCLIMATION(U) ARMY RESEARCH INST OF ENVIRONMENTAL MEDICINE NATICK MA M A KOLKA ET AL. 1/1

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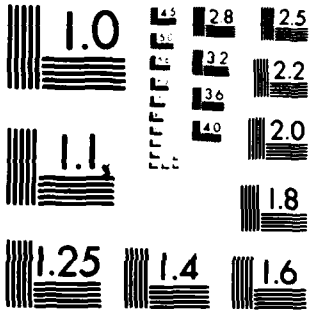

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HEAT EXCHANGE FOLLOWING ATROPINE INJECTION BEFORE AND AFTER HEAT ACCLIMATION

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Running head: heat exchange and atropine injection

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Abstract

The effect of saline and atropine injection (2 mg, im) on eight healthy, male subjects before and after heat acclimation was studied while each subject did treadmill walking (1.34 m • s^{-1}) in a hot-dry environment (T_a = 48.4°C, T_{dp} = 20.5°C). Partitional calorimetric analysis was done for the periods in which maximum sweat inhibition occurred (30 min). Mean skin temperature ($\bar{T}_{sk}$), rectal temperature (T_{re}), and heart rate were continuously observed. Evaporative loss from the skin (E_{sk}) was calculated by changes in body weight (Sauter balance); heat transfer coefficients were defined by Nishi equations. A prediction of sweat inhibition based on an analysis of heat storage (ΔT_{stor}) and its effect on a theoretical temperature (T_{act}), which can be graphed on a psychrometric chart, was developed. A rational effective temperature (ET*) defined as the T_0 at the intersection of the 50% rh which encompasses total heat exchange was used to compare the effects of atropine before and after heat acclimation. The results show that heat acclimation reduced ET* by some 2.5°C when compared to the unacclimated state after atropine injection. Thus, heat acclimation reduces the hazards of heat stroke caused by exercise in the heat with atropine injection.

key words: antimuscarinic drugs; exercise; heat acclimatization; mean body temperature; rational effective temperature; sweating rate

Antimuscarinic drugs such as atropine are becoming useful in acute treatment of anticholinesterase poisoning and in chronic disorders such as peptic ulcer or Parkinsonism (9). The competition by atropine for similar receptor sites on the eccrine sweat glands results in a transient blockage of the efferent signal from the central nervous system. This effect, systematically, reduces thermoregulatory sweating and eventual evaporative heat loss causing intense heat storage leading to frank hyperpyrexia (2,8).

The mechanisms involved in heat acclimation of humans have been shown to cause either potentiation of specific sweat gland activity (3) or, in passive heating or wet-heat, lowering of the internal body temperature reference point without changes in sweat-gland responsivity (4,7). Although the pattern of change in various other physiological indices during heat acclimation is well understood, no general biophysical model is presently available that describes the alteration in heat balance during both atropine injection and heat acclimation. Heat exchange properties have been adequately depicted graphically (6,11,12) as a function of two independent variables: operative temperature (T_o) and ambient vapor pressure (P_a). This approach requires only an adequate measurement of convective, radiative and evaporative heat transfer and a knowledge of net heat flow through the skin. This paper reports on the development of a method for the assessment of heat exchange properties used to quantify the combined effects of atropine injection and heat acclimation.

METHODS

Subjects - Eight males volunteered for the study following consent procedures passed by the U.S. Army Human Investigative Committee. The subjects had an average ($\pm$SD) age of 22 $\pm$ 3, weight of 79.9 $\pm$ 9.8 kg, Dubois surface area of 2.02 $\pm$ 0.16, and % body fat (hydrostatic weighing method) of 14.6 $\pm$ 4.6; $\dot{V}O_2$ max of the subjects was 50.2 $\pm$ 6 ml $\cdot$ kg^{-1} $\cdot$ min^{-1}.

Protocol - Testing occurred in a tropic/wind chamber during March through May. All subjects were tested with the drug injection prior to heat acclimation and after a period of 10 days of heat exposure. Heat acclimation (49°C/20% rh) was confirmed when rectal temperature and/or heart rate had levelled off. All 8 subjects walked on a treadmill set at 1.34 $m \cdot s^{-1}$ (metabolic rate about 360 W). The subjects were in good health and had not taken any prescribed or unprescribed medication or alcohol during the course of the experiments.

Each subject completed the exercise-heat exposure twice during the pre-acclimation period. On one occasion, 2 mg. of atropine sulphate was injected into the vastis lateralis immediately before the subjects entered the environmental chamber (15 min before the onset of exercise). The second pre-acclimation exposure involved the injection of an identical volume of sterile saline (im). These exposures were randomized and separated by at least 2 days to avoid possible carry-over effects of acute heat exposure. The post-acclimation testing was identical to the pre-acclimation testing; once after the injection (im) of atropine sulfate and again after the im injection of sterile saline. These exposures were randomized and separated by one day.

Physiological variables

The testing consisted of an exercise-heat exposure (25% $\dot{V}O_2$ max, T_a = 48.4°C, and T_{dp} = 20.5°C) in which the subjects attempted to walk (1.34 $m \cdot s^{-1}$) on a level for repeated bouts of 10 min rest, 25 min exercise until voluntary termination or 140 min elapsed. Rectal and mean skin temperature (3 sites) and heart rate were continuously monitored. Metabolic heat production was calculated by open-circuit spirometry. Total body sweat rates were determined from weight changes, each 25 min utilizing a Sauter balance ($\pm$ 0.005 kg). Subjects drank water ad libitum during all heat exposures.

Environmental Variables and Theory of Components of Heat Exchange Model

The basic environmental measurements were dry bulb (T_a) and dew point temperature (Eastern Instruments, Inc.); indices such as black globe (T_g) and wet globe (T_{wg}) were also monitored throughout the experiment. Wind speed was set at 1.21 $\pm$ .09 m $\cdot s^{-1}$. All tests were at a constant T_a of 48.4°C $\pm$ 0.9 and T_{dp} of 20.5°C $\pm$ 1.9.

This paper encompasses elements of heat exchange calculated after 30 min post im injection of 2 mg atropine or saline in subjects completing the full exercise bout. Metcalfe (9) has shown that plasma levels of atropine in humans after im injection of 2 mg have peak plasma levels of 16.4 n moles $\cdot l^{-1}$ occurring at about 20 min with a 50% fall off of peak level around 3 h.

A heat balance relating all environmental and physiological factors during the 30th min was done in which:

$$S = M_{sk} - \text{(sensible heat loss)} - \text{(skin evaporation)} \qquad \text{eq 1}$$

or $$S = M_{sk} - hF_{cl}(\bar{T}_{sk} - T_o) - wh_e F_{pcl}(P_{s'sk} - P_a) \qquad \text{eq 2}$$

where S is the rate of body heat storage ($W \cdot m^{-2}$); +, if increasing compared to resting state after atropine injection or to the combined effects of heat stress.

$P_{s,sk}$ is the saturation vapor pressure at $\bar{T}_{sk}$ (Torr)

P_a is the ambient vapor pressure (Torr) calculated from dew point

w is the equivalent fraction of the total body surface (A_D) wet with sweat which was calculated from $E^*\lambda / E_{max}$ (6,10) where E_{max} is the maximum evaporative power of the environment: 2.2 h_c ($P_{s,sk} - P_a$). The average heat transfer coefficient (h_c) was calculated from Nishi and Gagge (10) originally done in this chamber during treadmill walking. The net heat flow (M_{sk}) was determined from $M-E_{res}-C_{res}$; the latter are respired and dry heat loss from the lungs (10). The factors F_{cl} and F_{pcl} in eq 2 are clothing efficiency factors for dry

heat transfer and water vapor permeation (10). For our subjects these were 0.79 and 0.88, respectively for the I_{clo} of 0.15 worn.

Equation 2 above may be rewritten in terms of two gradients (12) in which

$$P_a - P_{s,sk} = (-\psi/w)\ T_o - (T_{act} + \Delta T_{stor}) \qquad \text{eq 3}$$

where ψ encompasses the sensible to insensible heat losses $hF_{cl}/h_e F_{pcl}$ which includes clothing and air movement effects, Torr/°C

T_o is the operative temperature of the test chamber in which $T_o = (h_r \bar{T}_r + h_c T_a)/(h_r + h_c)$. (5)

$\bar{T}_r$ was evaluated from $T_g + 2.2\sqrt{V}(T_g - T_a)$ in the chamber

One can derive an additional factor for our analysis from eq 3. This is the theoretical temperature (T_{act}) at which each of the subjects, for the given metabolic activity, would be at thermal equilibrium without evaporative heat loss:

$$T_{act} = \bar{T}_{sk} - M_{sk}/hF_{cl} \qquad (^{o}C) \qquad \text{eq 4}$$

This T_{act} is affected when each of the subjects store heat as the sweat glands were inhibited by atropine injection. The maximum inhibition would theoretically occur when plasma levels were highest (20 min) (9).

We propose that numerical values of this effect can be quantified by ΔT_{stor} in eq 3 which is proportional to rate of rise in mean body temperature, ($\bar{T}_b$) as:

$$\Delta T_{stor} = S/hF_{cl} = (\Delta \bar{T}_b/\Delta t) \cdot [(0.97 * m_b)/A_D]/hF_{cl}, \qquad (^{o}C)$$

where 0.97 is specific heat constant ($W \cdot h \cdot kg^{-1} \cdot {}^{o}C^{-1}$)

and $\dot{m}_b$ is body mass (lean), A_D is surface area, m^2.

Equation 2 may be represented on a psychrometric chart by a series of straight lines which pass through a common point (CP). The effect of body heating due to atropine or an unacclimated state is to cause a rate of

displacement (right of the X-axis) of the common point with Cartesian coordinates of (T_{act} + Δ T_{stor}, $P_{s,sk}$) through which a negative slope (ψ) line can be drawn. The rate of displacement, Δ T_{stor} is proportional to body heating effects of atropine for the pre- and post-heat acclimated state. OP represents the environmental conditions (T_o, P_a) to which the subjects were exposed. The line connecting CP and OP at the intersection of the 50% rh curve on a psychrometric chart represents an effective temperature (ET*) defined by T_o useful for predicting efficacy of heat acclimation (6,11) in reducing the effects of atropine on sweat gland inhibition at a given time of exposure. Although ET* is a theoretical temperature of an isothermal enclosure in which a person would exchange the same total heat by (R + C) and E_{sk}, it nevertheless numerically quantifies a summed effect of the heat stress. It is composed of the combined effects of T_o, P_a and physiological strain and changes in heat balance by atropine injection.

RESULTS

Table 1 summarizes the average values of the environmental and physiological variables after equivalent 30-min exposures following atropine injection. The effects of atropine injection are clearly evident by the decreases in skin wettedness levels (E_{sk}/E_{max}) compared to the similar exposures but with saline injections. Also evident is the resultant effect of body heating (Δ T_{stor}) from inhibition of sweating after atropine which caused a 45% increase in the effective T_{act} owing to storage of heat in those individuals unacclimated to heat; only a 30% increase occurred in those heat-acclimated.

Based on the observed data in Table 1, a practical psychrometric chart has been developed in Fig. 1A and B, for the 3-4 met activity level. These charts show that heat acclimation lowers the effective temperature (intersection of 50% rh line) by some $1^{o}C$ in comparison to unacclimated state following saline

placebo. The heat acclimated state, however, reduced the ET* by some 2.5°C when compared to unacclimated state following atropine injection.

DISCUSSION

Our analysis shows that as a practical application, hazard of heat stroke caused by work-in-the-heat routines following antimuscarinic drug application can be effectively reduced by heat acclimation (1,2,8). Heat acclimation also has the consequent effect of reducing the effective temperature (ET*) which is uniquely related to the mean skin temperature, skin wettedness and body core temperature. One variable which was not adequately handled was the relationship between the transfer characteristic ψ and skin wettedness levels. In normal circumstances (Table 2) Gagge and Nishi (5) have shown that typical environmental/work situations at 3 mets give a ψ of 0.7 and are comparable to our values when the skin is fully wetted.

Table 2.Probable ψ/w for various degrees of heat stress

	comfortable	minor strain	major strain
ψ/w	0.71/0.2	0.71/0.4	0.71/0.9

or $100 \cdot \psi$ HSI

Usually skin wettedness of 0.2 (or Belding - Heat Stress Index of HSI/100) is associated with acceptable environments whereas a 0.35 to 0.60 would cause minor strain (1). In the present experimental situation, the effect of atropine caused markedly decreased skin wettedness levels compared to the values with saline injection. The potentiation of (R+C) with heat acclimation or efficiency of the peripheral circulation during exercise would have to occur to result in a smaller ΔT_{stor}. Such an effect would allow the heat elimination of a given M_{sk}/hF_{cl} from the body when E_{sk} is depressed at a given constant E_{max} which

likely occurs during the atropine injection following a heat acclimatized condition. Interestingly, in this study once the subjects were able to overcome the transient effects of atropine injection, heat acclimation also improved total work time (59.5 $\pm$ 13.9 min atropine pre-heat acclimation versus 79.3 $\pm$ 41 min atropine post-heat acclimation). Unlike Craig et al's study (2), our responses would concur with Metcalfe's observations (9) concerning the time course in plasma atropine concentration levels. He showed that plasma levels of atropine drop to about 50% of peak levels after 3 h. Thus, with a higher liberation of acetycholine by a greater efferent drive to the sweat gland, less receptors typically are available which become blocked by a given dose of atropine. The effects of 2 mg injection of atropine would likely be marginal after 2 h if the person is heat acclimatized adequately.

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The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as official Department of the Army position, policy or decision, unless so designated by other official documentation.

Human subjects participated in these studies after giving their free and informed voluntary consent. Investigators adhered to AR 70-25 and USAMRDC Regulation 70-25 on Use of Volunteers in Research.

Table 1. Physiological responses (means $\pm$ 1 SD) and heat exchange properties following atropine injection (2 mg)

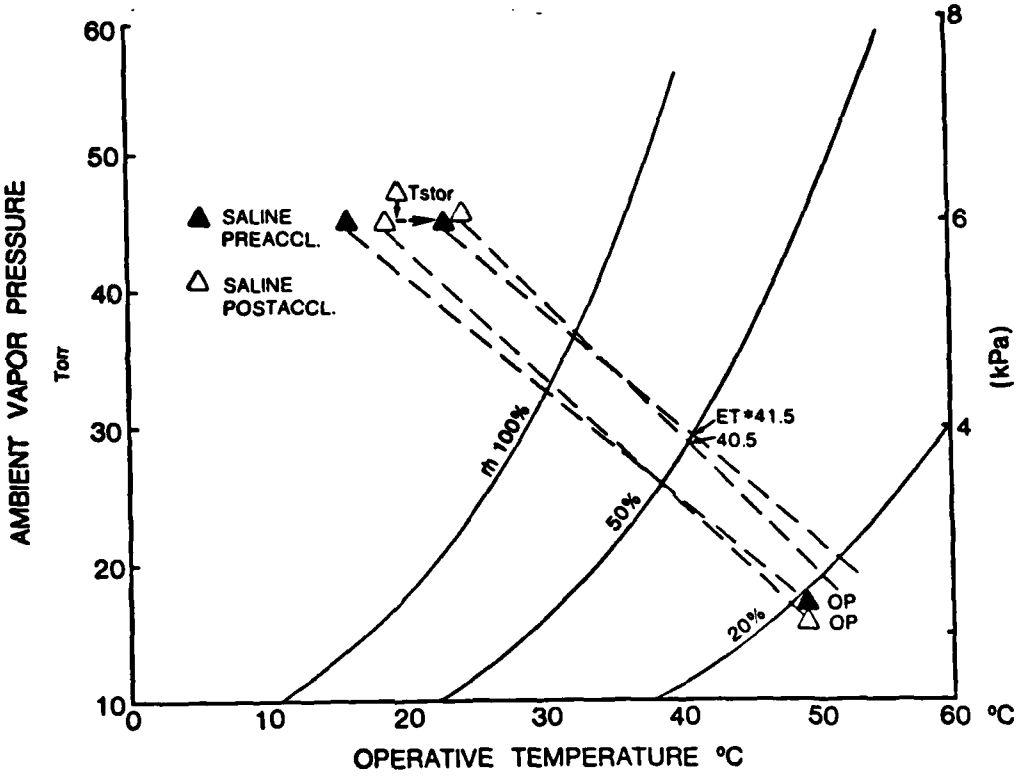
	T_{re} °C	$\bar{T}_{sk}$ °C	HR $b \cdot min^{-1}$	w %	*common point (T_{act}, $P_{s,sk}$)	ΔT_{stor} °C	$[T_{act} + \Delta T_{stor}$ °C$]$
Atropine Pre-Heat Acclimation	37.9 $\pm$0.5	38.8 $\pm$0.8	163 $\pm$12	28	20.6, 51.9	+12.7	33.3
Atropine Post-Heat Acclimation	37.8 $\pm$0.2	38.1 $\pm$0.7	160 $\pm$15	30	18.9, 50.1	+11.0	29.9
Saline Pre-Heat Acclimation	37.4 $\pm$0.2	36.1 $\pm$0.9	111 $\pm$9	52	16.9, 45	+ 5.8	22.9
Saline Post-Heat Acclimation	37.2 $\pm$0.2	36.1 $\pm$0.8	99 $\pm$13	60	17.9, 45	+5.3	23.2

*$T_{act} = \bar{T}_{sk} - M_{sk}/hF_{cl}$; w is skin wettedness from E_{sk}/E_{max}.

FIGURE LEGENDS

1A. ET^* loci in control (saline) experiments, pre- and post-heat acclimation.

1B. ET^* loci on a psychrometric chart following atropine injection, pre- and post-heat acclimation. P_{sk} is the skin saturation vapor pressure.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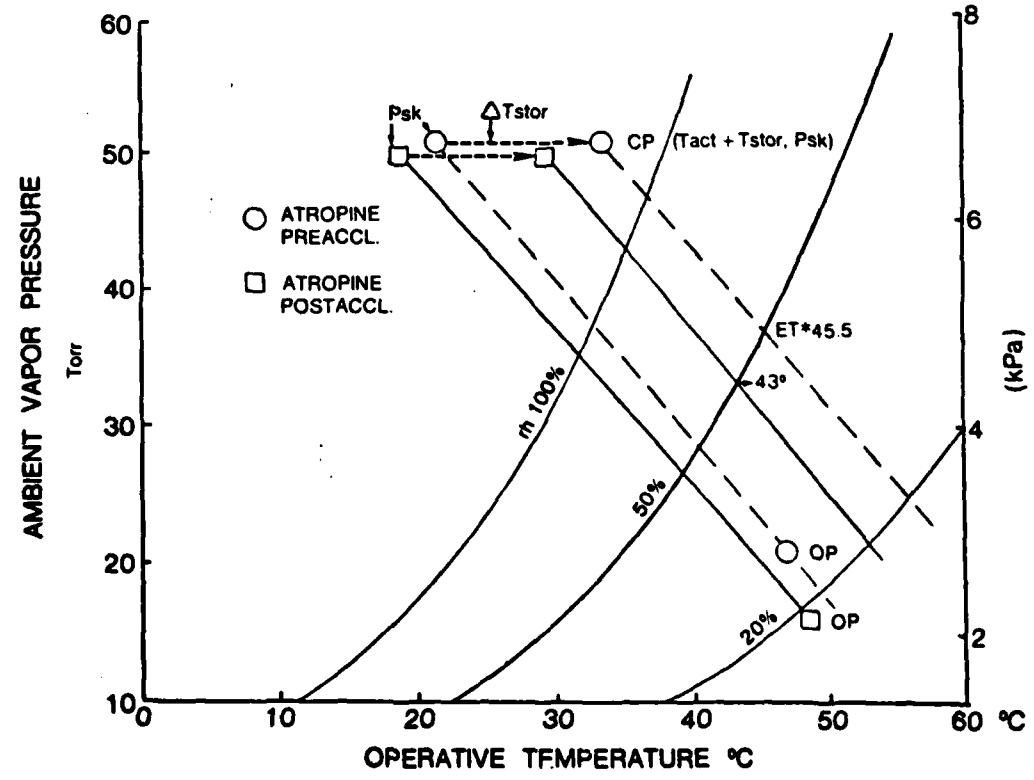
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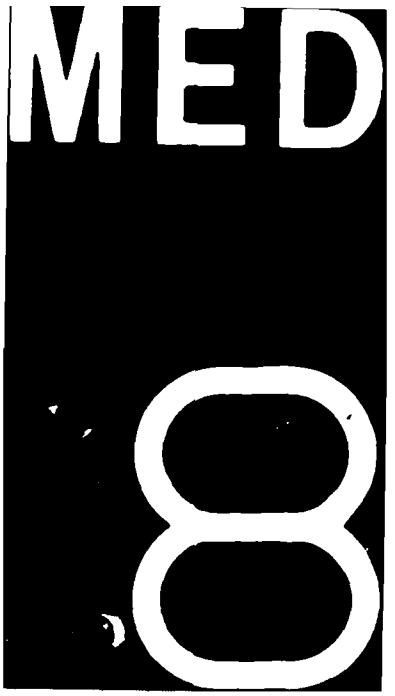
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